

Short communication

IgE-mediated hypersensitivity to latex in childhood

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A total of 267 children scheduled to receive anesthesia during a surgical, neurosurgical, or orthopedic intervention were investigated. IgE antibodies against latex were detected in serum samples of 6.4% (17/267 children) of the patients. The most important difference between sensitized and nonsensitized children was the number of surgical interventions in the past. The median of surgical interventions was 1.0 in the nonsensitized group of children and 3.0 in the sensitized group. Only 0.9% of the children with up to two surgical interventions and 34.1% with three or more procedures were sensitized to latex. Only one of the sensitized children developed intraoperative anaphylaxis during intervention after our investigation. We conclude that children with a history of three or more surgical interventions have a high risk of sensitization to latex proteins. Nevertheless, the predictive value of IgE antibodies against latex for development of anaphylaxis during anesthesia seems to be low.

Key words: children; IgE-mediated hypersensitivity; latex allergy.

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Latex allergy is a growing occupational problem. Recently published studies report that allergy to latex in hospital personnel may be as high as 17% (1–6). A second risk group is children with congenital malformation; the prevalence of latex allergy in children with spina bifida or myelomeningocele is up to 60% and is thought to be due to repeated surgical interventions and mucosal contact with latex (7–15). In contrast, Golden et al. reported that repeated surgical interventions did not correlate with a higher risk of latex sensitization in adults (16).

Comparing the data of 150 adults and nine children (age <14 years) with the diagnosis of latex allergy, we observed a significant difference in the number of surgical interventions in the past: an average of 2.8 surgical procedures in adults and an average of 7.3 procedures in children. The purpose of our study was to evaluate latex sensitization in children in relation to surgical history.

Material and methods

Patients

After approval of the study protocol by the ethics committee of the University of Münster, we investi-

gated, in a prospective study, 267 consecutive children (age <14 years) undergoing systemic anesthesia between November 1994 and April 1995 due to a surgical procedure in the department of pediatric surgery. Parents were interviewed by the participating anesthetist about history of atopic diseases, number of surgical interventions, and symptoms after contact with latex. A blood sample was taken during induction of anesthesia, and sera were stored at –20°C until investigation. Parents of latex-sensitized children were informed by letter and asked to allow skin prick tests.

IgE and specific IgE

Total IgE concentration and allergen-specific IgE antibodies were analyzed with the CAP-FEIA System (Pharmacia, Freiburg, Germany) according to the manufacturer's instructions. Values of allergen-specific IgE above 0.35 kU/l were considered positive.

Skin tests

Skin prick tests were performed with self-prepared latex solution, highly ammoniated latex (gift from

Regent Hospital Produkte, Mönchengladbach, Germany), and glove extracts.

Freshly collected latex of Malaysian rubber trees (*Hevea brasiliensis*) was preserved by adding ammonia and stored at 4°C. The solution was dialyzed against NaCl solution (0.9%), a membrane with cutoff of 1 kDa being used, and diluted 1:10 (v:v) with 0.9% NaCl. For preservation, phenol was added (0.4%). Prick tests were performed on more than 200 latex-allergic patients. Results were compared with prick tests using commercial latex solutions and highly ammoniated latex (gift from various glove manufacturers); sensitivity was about 94% (unpublished data).

Latex glove extracts were produced by shaking glove pieces (Peha-taft glove, Hartmann; Biogel glove, Regent) in 0.9% NaCl solution overnight. After centrifugation, the liquid phase was filtered through a 0.22-µm membrane, and phenol was added in a final concentration of 0.4% (w/v).

Skin prick tests were carried out on the volar side of the forearm. The largest diameter of the wheal was measured 20 min after the puncture. A wheal diameter greater than 2–3 mm was considered positive. 0.1% Histamine hydrochloride solution was used as positive and 0.9% NaCl with 0.4% phenol as negative control.

Glove-exposure test

The glove-exposure test was done by placing a Regent Biogel glove (low protein content) on one finger and subsequently a powdered Peha-taft Hartmann glove (high protein content) (17) on another for a maximum time of 30 min. Symptoms were observed for 1 h.

RAST inhibition test

The RAST-inhibition test was carried out by preincubating 50 µl serum of each patient with different amounts of the aqueous phase of centrifuged latex extract, followed by determination of latex-specific IgE antibodies with the CAP-FEIA System. The extent of inhibition of IgE binding was evaluated by comparing the values after preincubation with either NaCl solution (0.9%) or latex extract.

IgE Western blot

By the Western blot technique, we analyzed 16 of the 17 CAP-FEIA-positive serum samples. Nitrocellulose membrane with separated latex proteins (nonammoniated latex) (AlaSTAT AlaBLOT specific IgE test lot. no. ABUN 40/DPC, Los Angeles, CA, USA) were incubated overnight at 4°C with patient serum. After washing with PBS, alkaline

phosphatase-labeled antihuman IgE antibody was added. Visible bands indicating IgE-reactive bands were produced by developing in NBT/BCIP as substrate. Test procedures and calculation of molecular weights of allergens were carried out according to the manufacturer's instructions.

Statistical analysis

Data were analyzed by SPSS software. The chi-square test and Fisher's exact test were used for qualitative variables. Total serum IgE levels were analyzed by the Kruskal-Wallis test, and children's age by the Mann-Whitney test.

Results

A total of 184 (68.9%) children were male and 83 (31.1%) were female. Ages ranged from 0.2 to 14 years (median 5.4, standard deviation 3.8). Two children (0.75%) suffered from spina bifida. Latex-specific IgE antibodies were detected in 17/267 sera (6.4%); these patients were termed "sensitized". Antibody concentrations ranged from 0.36 kU/l (CAP class 1) to >100 kU/l (CAP class 6). Between the sensitized and nonsensitized children, no significant differences of age ($P = 0.7$) and sex ratio ($P = 0.8$) were observed. In contrast, latex-sensitized children had highly significantly elevated levels of total serum IgE ($P = 0.0001$) and significantly more frequently a history of atopic diseases ($P = 0.001$). The number of surgical procedures in sensitized and nonsensitized children was highly significantly different (Table 1). Only 0.9% of children with a history of 0–2 surgical procedures before our investigation but 34.1% of children with a history of three or more interventions ($P < 0.0001$) were sensitized to latex proteins (Table 2).

A skin prick test was performed in 8/17 latex-sensitized children, and the result was positive in seven patients. The glove-exposure test was

Table 1. Differences between nonsensitized and sensitized children

	Nonsensitized <i>n</i> = 250	Sensitized <i>n</i> = 17	<i>P</i>
Specific IgE (median)		2.52 kU/l	
Male/female	69.2%/30.8%	64.7%/35.3%	0.7
Age (median)	5.4 years	6.3 years	0.8
<5 years	45.2%	41.2%	
5–10 years	34.8%	41.2%	
10–14 years	20%	17.6%	
Total IgE (median)	16.5 kU/l	135 kU/l	0.0001
IgE > 100 kU/l	13.6%	64.7%	0.0001
Atopy (anamnestic)	9.6%	41.1%	0.001
History of surgical procedures (median)	1.0	3.0	<0.0001

Table 2. Relationship between number of surgical procedures and sensitization to latex

Surgical interventions	CAP class						Sum	Sensitized
	0	1	2	3	4	5	6	
0	120	1						
1	72		1				223	0.9%
2	29							
≥3	29	2	6	2	2	2	1	44
								34.1%

performed in five sensitized children, and local erythema was observed in three and also localized urticaria in one child.

Symptoms of latex allergy were reported only by two of the sensitized children:

- 1) A 4-year-old boy with history of atopic eczema had developed local urticaria after inflating toy balloons in the past. He did not suffer allergic reactions during a total of nine surgical procedures; in fact, proctoplasty was done without complications. Total IgE was 135 kU/l, latex-specific IgE was 1.6 kU/l, and skin prick tests with different latex solutions were positive; in the provocation test with a Regent Biogel glove we observed local erythema.
- 2) During peritoneoplasty after our investigation, a 6-year-old boy had bronchospasm, cardiovascular disorder, and cutaneous eruption. Symptoms of latex allergy had never been noted during four previous interventions for omphalocele. Total IgE was 240 kU/l, and latex-specific IgE 28.9 kU/l. The skin test with latex solutions was positive, and the glove provocation tests were tolerated without skin reactions.

RAST-inhibition tests were carried out in nine serum samples of latex-sensitized children (s-IgE >1 kU/l). Significant inhibition was found in eight of these (range 37.2–100%, median 91%, standard deviation 22.7). Only in one serum sample was inhibition not observed (latex-specific IgE was >100 kU/l; after dilution, it was 88.4 kU/l). Skin tests were not performed in this patient, and a history of latex allergy was not reported.

The Western blot technique detected IgE antibodies against several antigenic latex components in 13 sera (Fig. 1); with three sera, only faintly stained bands were visible, and one of these sera belonged to the 4-year-old boy reporting local urticaria after inflating toy balloons. Calculated molecular weights were in the range 12–121 kDa.

Discussion

In the present study on children who had undergone surgery, latex-specific IgE antibodies were

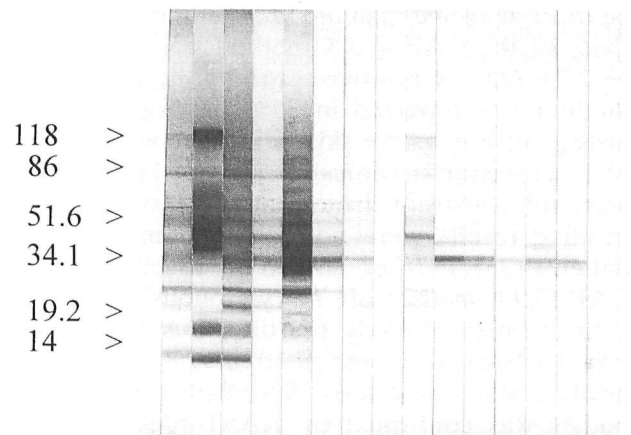


Fig. 1. Western blot analysis of IgE antibodies against latex in sera of 16 latex-sensitized children. Children reporting symptoms: lanes 1, 2 (left).

detected in 6.4% of 267 serum samples. The prevalence was 0.9% in children with a maximum of two surgical procedures in the past; this is in the range of the prevalence in other populations, mostly tested under suspicion of atopic symptoms (22). A significantly higher prevalence of 34.1% in children with a history of three or more procedures was in the range reported for children with spina bifida (7–15). The high frequency of latex allergy in those children is thought to be due to medical treatment, but a correlation between latex allergy and surgical history was reported only in some of these studies (7–15), and was negative in the general adult population (16).

Anaphylaxis during general anesthesia occurs with a frequency of 1/6000–1/30 000 procedures. Muscle relaxants are by far the worst offenders (18, 19), but anaphylactic shock in children during surgical procedures is mostly related to latex allergy (20). Gold et al. reported about 15 patients with spina bifida or congenital urologic abnormalities who collectively had experienced 19 intra-operative anaphylactic reactions (21). Of 17 latex-sensitized preoperative children in the present study, only one 6-year-old boy suffered from intra-operative anaphylactic reaction during the following procedure. None of the other 16 sensitized children suffered from anaphylaxis during intervention after our investigation, although they were not treated under latex-free conditions. In the literature, clinically relevant allergy to latex is reported consistently to vary between 0 and 75% in sensitized children with spina bifida, and only some of them suffered from anaphylaxis during surgical procedures (7–15).

In our study, we used the CAP-FEIA System to detect latex-specific IgE antibodies. It should be noted that skin tests with latex are considered to

be more sensitive than *in vitro* methods. The sensitivity of the CAP-FEIA method was reported to be 77% (23). A positive result by the CAP-FEIA method was reported in 30% of atopic patients instead of a negative skin prick test with a panel of latex extracts; clinically relevant latex allergy was not apparent from patient history. False-positive results were not observed in nonatopic patients (23). Further data on the specificity of the CAP-FEIA method are not yet published.

In the present study, the diagnosis of sensitization to latex was confirmed in 7/8 children by positive skin prick tests. Specificity of IgE antibodies was confirmed by RAST-inhibition tests. IgE antibodies against several latex components were demonstrated by Western blot analysis with sera of the latex-sensitized children. The calculated molecular weights of allergens recognized by IgE antibodies in children's serum were slightly lower than those reported for major allergens (7). One allergen with a calculated molecular weight of about 25 kDa was detected strongly by eight sera, and faintly by the others. We suggest that this band shows an anti-27-kDa antibody reported to be typical for children with multiple operations (7).

Many reports of latex allergy concern atopic patients (24). In the study of Turjanmaa, 67% of the latex-allergic employees had a personal history of atopy (1). In our study, 41.1% of the latex-sensitized children had a history of rhinoconjunctivitis, asthma, or atopic eczema, in contrast to 9.6% of 250 patients who were not sensitized to latex.

Many investigators found that latex allergy among adults occurs mainly in women. The predominance of women in these populations is probably related to a more frequent professional or domestic exposure to latex. In the present study, we did not observe a sex-linked predominance.

We conclude that atopic children with a history of three or more surgical procedures have a high risk of sensitization to latex. Preoperative screening should be required in this group of children, but we note that only a few latex-sensitized patients suffer from anaphylactic shock during anesthesia. Only a few patients urgently need a completely latex-free environment during surgical interventions. Further studies must define the subgroup of latex-sensitized patients who are at high risk during anesthesia.

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